Cleburne, TX, Cleburne Muni, VOR/DME RNAV OR GPS RWY 33, Amdt 4

Note: The FAA published an Amendment in Docket No. 28286, Amdt No. 1677 to Part 97 of the Federal Aviation Regulations (VOL 60 FR No. 151 Page 40071; dated Monday August 7, 1995) under Section 97.23 effective 14 SEP 95 which is hereby amended as follows:

Jacksonville, FL. Craig Muni, should read VOR or GPS Rwy 32, Amdt 2, CANCELLED

Note: The FAA published an Amendment in Docket No. 28266, Amdt No. 1674 to Part 97 of the Federal Aviation Regulations (VOL 60 FR No. 136 Page 36349; dated Monday July 17, 1995) under Section 97.27 effective 14 SEP 95, which is hereby amended as follows:

Loris, SC. Twin City, should read NDB or GPS Rwy 26, Amdt 2, CANCELLED

[FR Doc. 95–21014 Filed 8–23–95; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 882

[Docket No. 93N–0027]

Neurological Devices; Effective Date of Requirement for Premarket Approval of Cranial Electrotherapy Stimulators

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the cranial electrotherapy stimulator (CES), a medical device. This action is being taken under the Medical Devices Amendments Act of 1976. Commercial distribution of this device must cease, unless a manufacturer or importer has filed with FDA a PMA for its version of the cranial electrotherapy stimulator device within 90 days of the effective date of this regulation.

EFFECTIVE DATE: August 24, 1995.

FOR FURTHER INFORMATION CONTACT: Janine M. Morris, Center for Devices and Radiological Health (HFZ–450), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–443–8517.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of September 4, 1979 (44 FR 51770), FDA published § 882.5800 (21 CFR 882.5800) classifying the CES into class III (premarket approval). Section 882.5800 applies to (1) Any CES that was in commercial distribution before May 28, 1976, the date of enactment of the Medical Devices Amendments of 1976 (the amendments) (Pub. L. 94–295), and (2) any device that FDA has found to be substantially equivalent to the CES and that has been marketed on or after May 28, 1976.

In the **Federal Register** of August 31, 1993 (58 FR 45865), FDA published a proposed rule to require the filing under section 515(b) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360e(b)) of a PMA or a notice of completion of a PDP for the CES. In accordance with section 515(b)(2)(A) of the act, FDA included in the preamble to the proposal the agency's proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the evice to meet the premarket approval requirements of the act, and the benefits to the public from use of the device (58 FR 45865 at 45867). The August 31, 1993, proposed rule also provided an opportunity for interested persons to submit comments on the proposed rule and the agency's proposed findings. Under section 515(b)(2)(B) of the act (21 U.S.C. 360e(b)(2)(B)), FDA also provided an opportunity for interested persons to request a change in the classification of the device based on new information relevant to its classification. Any petition requesting a change in the classification of the cranial electrotherapy stimulator was required to be submitted by September 15, 1993. The comment period closed on November 1, 1993.

FDA received two petitions requesting a change in the classification of the device from class III to class II. FDA reviewed the petitions and found them deficient based on the lack of new information that was relevant to the device's classification. Each petitioner was sent a deficiency letter dated February 4, 1994, requiring a response to the reported deficiencies. Both petitions were deemed closed August 23, 1994, based on the petitioners' lack of response.

II. Summary and Analysis of Comments and FDA's Response

The comments addressed issues relating to valid scientific studies pertaining to behavioral science and risks associated with the use of the CES device. (See 58 FR 46865 at 46867 and 46868 for a discussion of the benefits and risks of the CES device.) The comments are summarized as follows:

1. A few comments were concerned that FDA's proposed findings were not evaluated by qualified behavioral scientists who could read and understand the literature. The comments noted that several references cited in the proposal do not meet the behavioral science criteria of a reliable ''dependent vector'' and would not have appeared in a knowledgeable behavioral science review. The comments further noted that the review conducted by a National Research Council panel on Electrosleep and Electroanesthesia did not include any behavioral scientists, and 90 percent of the studies reviewed by the panel were behavioral science studies.

FDA recognizes that the proposed rule did not present critical reviews of all the literature. FDA also agrees that many of the studies in the literature do not meet the minimum criteria of behavioral science review. FDA has cited these publications only to show that the valid scientific evidence that is required to demonstrate the safety and effectiveness of CES devices in the form of well-controlled clinical studies is not presented in published data. FDA believes the data presented in the literature are not sufficient to fulfill the requirements of valid scientific evidence. Some of the studies were controlled studies that may have indicated some effect; however, information in the literature does provide a reasonable assurance that the device produces a reliable, repeated treatment effect. The few studies that presented controlled data were studying different clinical endpoints on a small number of patients so that an effect could not be established.

2. One comment said that the risks to health identified in the proposed rule (worsening of the condition being treated, potential risk of seizure, skin irritation, and blurred vision) appear exaggerated, as discussed below:

a. The comments said the risk of worsening of the condition being treated could easily be controlled by informing the patient when he or she should expect the treatment effect to occur. The comments stated that, for the case of a depressed patient, the perceived worsening effect is due to the patient's expectations for immediate effect.

FDA agrees that the risk of worsening of the condition being treated might be controlled. However, until the CES is proved effective through valid scientific evidence, the agency believes that patients should not be subjected to the risk of worsening their condition by an ineffective treatment.

b. One individual commented on personal involvement in a number of studies comprising a total of 800 patients where 26 of the patients were

known seizure patients, and no seizures were reported.

FDA observes that research relating electrical stimulation to epileptiform seizures has been studied only at higher levels of stimulation. The risk associated with the lower levels of electrical stimulation used with CES has not been systematically studied.

c. The same comment stated that over 10,000 users of CES devices manufactured in the United States have never reported a burn.

FDA agrees that there have been few reports of burns associated with CES devices; however, the device has the potential for causing burns. This risk appears to be unreasonable in the absence of established device effectiveness.

d. One comment stated that blurred vision as a risk factor should not be considered because of a misconception about how electrodes are placed. The comment states that placing electrodes over the eyes was an early Russian technique that was abandoned in the United States by 1970.

FDA agrees that risks, such as blurring of vision, could be minimized; however, the existence of these potential risks is cited as evidence that premarket approval is appropriate, particularly in the absence of established device effectiveness. FDA believes that it is not clear whether placing of electrodes is the sole cause of blurred vision.

3. One comment stated that the Weschler Adult Intelligence Scale and the Beta Examination Intelligence Quotient test are proven psychological measures of human intelligence.

FDA intended to convey that many of the study measures of treatment effect are subjective and may not be considered valid as sole measures. However, FDA believes that it should review the validity of other measures including psychological measures, in the form of a PMA to provide reasonable assurance of the safety and effectiveness of this device.

4. Another comment stated that the lack of followup data is not an adequate reason to invalidate a study reviewed in the literature because most of the studies were conducted by researchers who were not interested in study followup.

FDA agrees that the absence of followup data should not be the sole reason not to accept clinical data on CES. However, FDA believes followup data are important in evaluating the long-term effects of CES devices and are components that should be considered to determine the safety and effectiveness of this device.

5. One comment said that studies published by behavioral scientists include data that meet a statistical confidence of 95 percent and that their probability tables take into consideration whether the population is 5 or 500 subjects. The comment further stated that FDA was incorrect to say that the small sample size used in the study conducted by M. F. Weiss (58 FR 45865 at 45870 (Ref. 32)) would not demonstrate statistical significance for treatment effect.

FDA believes that there was not sufficient information to determine that the Weiss study demonstrated a statistically significant effect. In addition, a single study of 10 subjects is not adequate to support a repeatable effect for the purposes of determining the safety and effectiveness of this device.

6. One comment stated that FDA's review of the study by F. Ellison (58 FR 45865 at 45870 (Ref. 5)) in the proposal) was not complete. The comment said that Ellison's findings were that a single day of treatment was too short a duration to control withdrawal symptoms effectively and that 2 days of treatment were effective.

FDA agrees that the purpose of the second experiment was to determine if 24 hours of treatment was sufficient to show an effect and that the purpose of the first experiment was to determine if there was a treatment effect after 48 hours. However, FDA believes the conclusions made in Ellison's study were based on the premise that CES was effective treatment. Based on the data that were presented, FDA could not draw the same conclusions.

7. One comment stated that the references cited by V. Krauthamer (58 FR 45865 at 45870 (Refs. 14 and 15)) did not support the concept that electrical stimulation by CES is harmful.

FDA did not cite these references to show that CES is harmful. The references by Krauthamer addressing the risk of potential adverse effects from electrical stimulation of the brain were cited to show that the effects of electrical stimulation are still unknown and have not been systematically evaluated, particularly for lower levels of stimulation.

8. Several comments asserted that FDA did not review all the data available on CES devices. One comment referenced to four randomized controlled trials that were not cited in the references listed in the proposed rule. Another comment reported on data submitted to FDA in PMA's.

FDA attempted to review all the published data available in the United States, and referenced in the proposed rule those the agency believes to be the most significant studies. Because the comments did not include copies of the four studies referred to, or citations to them, FDA cannot determine whether these studies were reviewed. Regarding the data submitted to FDA under a PMA, these data are considered proprietary information and are not intended for public release. However, they may be submitted as part of a PMA in response to this final rule.

9. One comment submitted by a physician endorsed treating patients with addictions, and reported that CES has been a helpful adjunctive therapy in the treatment of psychoactive drug withdrawal syndromes.

FDA believes that the comment that CES is helpful as an adjunctive therapy in drug withdrawal is anecdotal and does not represent valid scientific evidence.

10. One comment objected to the fact that FDA did not make available to the public all references cited in the proposed rule at the Dockets Management Branch and requested an extension of the comment period for an additional 2 months.

FDA considered comments received after the close of the official comment period and believes, therefore, that there was a sufficient comment period in which manufacturers, physicians, consumer organizations, researchers, and individuals could comment and present new information to determine whether FDA has a reasonable basis to require PMA's or notices of completed PDP's for the CES. Copies of the references cited were put on display at the Dockets Management Branch within 7 days of the proposed rule's publication.

11. Two comments offered recommendations regarding the design of future studies to ensure high quality. One comment stated that published literature on CES devices has not shown through valid scientific evidence that these devices are effective.

FDA agrees that the current literature is not adequate to support the safety and effectiveness of CES's and welcomes all recommendations for future studies to determine the safety and effectiveness of CES's.

12. One comment stated that FDA's decision to require the submission of PMA's or notices of completed PDP's for CES devices is too costly and too time consuming.

FDA has examined the economic consequences of the rule. The agency believes that only a small number of firms will be affected by this final rule. FDA's mission to protect the public health requires that the safety and

effectiveness of these medical devices must be demonstrated.

FDA believes that the comments presented insufficient information on which to base special controls that could assure safety and effectiveness. The agency concludes that its proposed findings and its conclusion discussed in the preamble to the proposed rule are appropriate. Accordingly, FDA is issuing a final regulation requiring premarket approval of the CES under section 515(b)(3) of the act.

III. Final Rule

Under section 515(b)(3) of the act, FDA is adopting the findings as published in the preamble to the proposed rule and is issuing this final rule to require premarket approval of the generic type of device, the cranial electrotherapy stimulator device, by revising § 882.5800(c).

Under the final rule, a PMA or a notice of completion of a PDP is required to be filed with FDA within 90 days of the effective date of this regulation for any CES device that was in commercial distribution before May 28, 1976, or any device that FDA has found to be substantially equivalent to such a device on or before November 22, 1995. An approved PMA or declared completed PDP is required to be in effect for any such device on or before 180 days after FDA files the application. Any other CES device that was not in commercial distribution before May 28, 1976, or that FDA has not found, on or before November 22, 1995, to be substantially equivalent to a CES device that was in commercial distribution before May 28, 1976, is required to have an approved PMA or declared completed PDP or declared completed in effect before it may be marketed.

If a PMA or notice of completion of a PDP for a CES device is not filed on or before November 22, 1995, that device will be deemed adulterated under section 501(f)(1)(A) of the act (21 U.S.C. 351(f)(1)(A)), and commercial distribution of the device will be required to cease immediately. The device may, however, be distributed for investigational use, if the requirements of the investigational device exemption (IDE) regulations (21 CFR part 812) are met.

Under § 812.2(d) (21 CFR 812.2(d)) of the IDE regulations, FDA hereby stipulates that the exemptions from the IDE requirements in § 812.2(c)(1) and (c)(2) will no longer apply to clinical investigations of the CES device. Further, FDA concludes that investigational CES devices are significant risk devices as defined in § 812.3(m) and advises that as of the effective date of § 882.5800(c), requirements of the IDE regulations regarding significant risk devices will apply to any clinical investigation of a CES device. For any CES device that is not subject to a timely filed PMA or notice of completion of a PDP or notice of completion of a PDP, an IDE must be in effect under § 812.20 on or before November 22, 1995, or distribution of the device for investigational purposes must cease. FDA advises all persons currently sponsoring a clinical investigation involving the CES device to submit an IDE application to FDA no later than October 23, 1995, to avoid the interruption of ongoing investigations.

IV. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) and (e)(4) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because PMA's for this device could have been required by FDA as early as March 4, 1982, and because firms that distributed this device prior to May 28, 1976, or whose device has been found to be substantially equivalent to the CES in commercial distribution before May 28, 1976, will be permitted to continue marketing cranial electrotherapy stimulators during FDA's review of the PMA or notice of completion of the PDP, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

List of Subjects in 21 CFR Part 882

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 882 is amended as follows:

PART 882—NEUROLOGICAL DEVICES

1. The authority citation for 21 CFR part 882 continues to read as follows:

Authority: Secs. 501, 510, 513, 515, 520, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351, 360, 360c, 360e, 360j, 371).

2. Section 882.5800 is amended by revising paragraph (c) to read as follows:

§ 882.5800 Cranial electrotherapy stimulator.

* * * * *

(c) *Date a PMA or notice of completion of a PDP is required.* A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before November 22, 1995, for any cranial electrotherapy stimulator that was in commercial distribution before May 28, 1976, or that has on or before November 22, 1995, been found to be substantially equivalent to the cranial electrotherapy stimulator that was in commercial distribution before May 28, 1976. Any other cranial electrotherapy stimulator shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: July 31, 1995.

D. B. Burlington,

Director, Center for Devices and Radiological Health.

[FR Doc. 95–20960 Filed 8–23–95; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF LABOR

Occupational Safety and Health Administration

29 CFR Part 1952

Approved State Plans for Enforcement of State Standards; Approval of Supplements to the Nevada State Plan

AGENCY: Occupational Safety and Health Administration, Labor.

ACTION: Approval of supplements to the Nevada State Plan.